All references disclosed herein are incorporated by reference in their entirety.

I claim:

1. A fusion protein reporter comprising,

a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties.

2. The fusion protein reporter of claim 1, wherein the histone-modification specific binding domain is conjugated to the histone polypeptide with a linker molecule.

3. The fusion protein reporter of claim 1, further comprising one or more additional histone-modification-specific binding domains.

4. The fusion protein reporter of claim 1, wherein the histone polypeptide is selected from the group consisting of H3 and H4.

5. The fusion protein reporter of claim 1, wherein the histone polypeptide is selected from the group consisting of the N-terminus of H3 and the N-terminus of H4.

6. The fusion protein reporter of claim 1, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

7. The fusion protein reporter of claim 1, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

8. The fusion protein reporter of claim 1, wherein the histone modification is selected from the group consisting of acetylation, methylation, and phosphorylation.

9. The fusion protein reporter of claim 1, wherein the histone-modification-specific binding domain is selected from the group consisting of: 14-3-3, FHA, WW, bromodomain, and chromodomain.

10. The fusion protein reporter of claim 9, wherein the bromodomain comprises the amino acid sequence set forth as SEQ ID NO: 3.

11. The fusion protein reporter of claim 9, wherein the bromodomain is selected from the group consisting of: Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

12. The fusion protein reporter of claim 9, wherein the chromodomain is selected from the group consisting of : HP1, MRG15, MRG-1, cynCDY, Hrp3, dMi-2, CHD5, Swi6, and pdd3p.

13. The fusion protein reporter of claim 1, wherein the histone polypeptide is a polypeptide substrate for the histone-modification-specific binding domain.

14. The fusion protein reporter of claim 1, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR (SEQ ID NO:1).

15. The fusion protein reporter of claim 1, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18).

16. The fusion protein reporter of claim 1, wherein the histone polypeptide is an H4 polypeptide comprising the amino acid sequence set forth as SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

17. The fusion protein reporter of claim 1, further comprising a targeting polypeptide, associated with the fusion protein.

18. The fusion protein reporter of claim 17, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand and a nuclear localization sequence (NLS), nuclear export signal (NES), plasma membrane targeting signal, a histone binding protein, and a nuclear protein.

19. An expression vector comprising an expression cassette encoding a fusion protein reporter of claim 1.

20. A host cell transformed or transfected with the expression vector of claim 19.

21. A method of determining the level of histone modification in a biological sample comprising:

contacting a biological sample with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties, and

monitoring the level of fluorescence resonance energy transfer (FRET) in the biological sample as a measure of the level of histone modification in the biological sample.

22. The method of claim 21, wherein the biological sample is selected from the group consisting of cells and tissues.

23. The method of claim 22, wherein the biological sample is a cell.

24. The method of claim 23, wherein the cell is undergoing cell division.

25. The method of claim 21, wherein the histone-modification specific binding domain is conjugated to the histone polypeptide with a linker molecule.

26. The method of claim 21, wherein the fusion protein reporter, further comprises one or more additional histone-modification-specific binding domains.

27. The method of claim 21, wherein the histone polypeptide is selected from the group consisting of H3 and H4.

28. The method of claim 21, wherein the histone polypeptide is selected from the group consisting of the N-terminus of H3 and the N-terminus of H4.

29. The method of claim 21 wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

30. The method of claim 21, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

31. The method of claim 21, wherein the histone modification is selected from the group consisting of acetylation, methylation, and phosphorylation.

32. The method of claim 21, wherein the histone-modification-specific binding domain is selected from the group consisting of: 14-3-3, FHA, WW, bromodomain, and chromodomain.

33. The method of claim 32, wherein the bromodomain comprises the amino acid sequence set forth as SEQ ID NO: 3.

34. The method of claim 32, wherein the bromodomain is selected from the group consisting of: Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

35. The method of claim 32, wherein the chromodomain is selected from the group consisting of : HP1, MRG15, MRG-1, cynCDY, Hrp3, dMi-2, CHD5, Swi6, and pdd3p.

36. The method of claim 21, wherein the histone polypeptide is a polypeptide substrate for the histone-modification-specific binding domain.

37. The method of claim 21, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR (SEQ ID NO:1).

38. The method of claim 21, wherein, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18).

39. The method of claim 21, wherein the histone polypeptide is an H4 polypeptide comprising the amino acid sequence set forth as SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

40. The method of claim 21, wherein the fusion protein reporter further comprises a targeting polypeptide, associated with the fusion protein.

41. The method of claim 40, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand and a nuclear localization sequence (NLS), nuclear export signal (NES), plasma membrane targeting signal, a histone binding protein, and a nuclear protein.

42. The method of claim 21, further comprising:

monitoring a subsequent second level of FRET in the biological sample, and comparing the first and second levels of FRET as a measure of the change in the level of histone modification in the biological sample.

43. The method of claim 21, further comprising:

comparing the level of fluorescence resonance energy transfer (FRET) in the biological sample to a control level of FRET as a determination of a histone modification disorder in the biological sample.

44. The method of claim 43, wherein the biological sample is from a subject and the determination of a histone modification disorder in the biological sample is diagnostic for a histone modification disorder in the subject.

45. The method of claim 43, wherein the control level of FRET is the level of FRET in a biological sample free of a histone-modification disorder.

46. A method of monitoring the onset, progression or regression of a histone-modification disorder in a subject comprising,

contacting a first biological sample obtained from a subject with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain

conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties,

determining the level of fluorescence resonance energy transfer (FRET) in the first biological sample,

contacting a subsequent second biological sample obtained from the subject with the fusion protein reporter,

determining the amount of FRET in the second biological sample,

comparing the level of FRET in the first biological sample to the level of FRET in the second biological sample as a measure of the onset, regression or progression of a histone modification disorder in the subject.

47. The method of claim 46, further comprising administering after the first biological sample is obtained from the subject and before the second biological sample is obtained from the subject, a candidate pharmacological agent to the subject, wherein the measure of the onset, regression, or progression of a histone modification disorder in the subject is an indication of the effect of the candidate pharmacological agent on histone modification in the subject.

48. The method of claim 46, wherein the biological sample is selected from the group consisting of tissue and cells.

49. The method of claim 46, wherein the histone-modification specific binding domain is conjugated to the histone polypeptide with a linker molecule.

50. The method of claim 46, wherein the fusion protein reporter, further comprises one or more additional histone-modification-specific binding domains.

51. The method of claim 46, wherein the histone polypeptide is selected from the group consisting of H3 and H4.

52. The method of claim 46, wherein the histone polypeptide is selected from the group consisting of the N-terminus of H3 and the N-terminus of H4.

53. The method of claim 46, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

54. The method of claim 46, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

55. The method of claim 46, wherein the histone modification is selected from the group consisting of acetylation, methylation, and phosphorylation.

56. The method of claim 46, wherein the histone-modification-specific binding domain is selected from the group consisting of: 14-3-3, FHA, WW, bromodomain, and chromodomain.

57. The method of claim 56, wherein the bromodomain comprises the amino acid sequence set forth as SEQ ID NO: 3.

58. The method of claim 56, wherein the bromodomain is selected from the group consisting of: Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

59. The method of claim 56, wherein the chromodomain is selected from the group consisting of : HP1, MRG15, MRG-1, cynCDY, Hrp3, dMi-2, CHD5, Swi6, and pdd3p.

60. The method of claim 46, wherein the histone polypeptide is a polypeptide substrate for the histone-modification-specific binding domain.

61. The method of claim 46, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR (SEQ ID NO:1).

62. The method of claim 46, wherein, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18).

63. The method of claim 46, wherein the histone polypeptide is an H4 polypeptide comprising the amino acid sequence set forth as SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

64. The method of claim 46, wherein the fusion protein reporter further comprises a targeting polypeptide, associated with the fusion protein.

65. The method of claim 64, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand and a nuclear localization sequence (NLS), nuclear export signal (NES), plasma membrane targeting signal, a histone binding protein, and a nuclear protein.

66. A method for evaluating the effect of candidate pharmacological agents on histone modification in a biological sample, comprising:

contacting a biological sample with a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties,

determining a first level of fluorescence resonance energy transfer (FRET) in the biological sample,

contacting the biological sample with a candidate pharmacological agent,

determining a second level of FRET in the biological sample, and

comparing the first level of FRET in the cell with the second level of FRET in the cell, wherein a relative increase or relative decrease in FRET indicates an effect of the candidate pharmacological agent on histone modification in the biological sample.

67. The method of claim 66, wherein the biological sample is selected from the group consisting of cells and tissues.

68. The method of claim 66, wherein the histone-modification specific binding domain is conjugated to the histone polypeptide with a linker molecule.

69. The method of claim 66, wherein the fusion protein reporter, further comprises one or more additional histone-modification-specific binding domains.

70. The method of claim 66, wherein the histone polypeptide is selected from the group consisting of H3 and H4.

71. The method of claim 66, wherein the histone polypeptide is selected from the group consisting of the N-terminus of H3 and the N-terminus of H4.

72. The method of claim 66, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

73. The method of claim 66, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

74. The method of claim 66, wherein the histone modification is selected from the group consisting of acetylation, methylation, and phosphorylation.

75. The method of claim 66, wherein the histone-modification-specific binding domain is selected from the group consisting of: 14-3-3, FHA, WW, bromodomain, and chromodomain.

76. The method of claim 75, wherein the bromodomain comprises the amino acid sequence set forth as SEQ ID NO: 3.

77. The method of claim 75, wherein the bromodomain is selected from the group consisting of: Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

78. The method of claim 75, wherein the chromodomain is selected from the group consisting of : HP1, MRG15, MRG-1, cynCDY, Hrp3, dMi-2, CHD5, Swi6, and pdd3p.

79. The method of claim 66, wherein the histone polypeptide is a polypeptide substrate for the histone-modification-specific binding domain.

80. The method of claim 66, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR (SEQ ID NO:1).

81. The method of claim 66, wherein, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18).

82. The method of claim 66, wherein the histone polypeptide is an H4 polypeptide comprising the amino acid sequence set forth as SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

83. The method of claim 66, wherein the fusion protein reporter further comprises a targeting polypeptide, associated with the fusion protein.

84. The method of claim 83, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand and a nuclear localization sequence (NLS), nuclear export signal (NES), plasma membrane targeting signal, a histone binding protein, and a nuclear protein.

85. A kit for diagnosing a histone-modification disorder, comprising:

a container containing a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties, and

instructions for the use of the fusion protein reporter in the diagnosis of a histone-modification disorder.

86. The kit of claim 85, wherein the histone-modification specific binding domain is conjugated to the histone polypeptide with a linker molecule.

87. The kit of claim 85, wherein the fusion protein reporter, further comprises one or more additional histone-modification-specific binding domains.

88. The kit of claim 85, wherein the histone polypeptide is selected from the group consisting of H3 and H4.

89. The kit of claim 85, wherein the histone polypeptide is selected from the group consisting of the N-terminus of H3 and the N-terminus of H4.

90. The kit of claim 85, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

91. The kit of claim 85, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

92. The kit of claim 85, wherein the histone modification is selected from the group consisting of acetylation, methylation, and phosphorylation.

93. The kit of claim 85, wherein the histone-modification-specific binding domain is selected from the group consisting of: 14-3-3, FHA, WW, bromodomain, and chromodomain.

94. The kit of claim 93, wherein the bromodomain comprises the amino acid sequence set forth as SEQ ID NO: 3.

95. The kit of claim 93, wherein the bromodomain is selected from the group consisting of: Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

96. The kit of claim 93, wherein the chromodomain is selected from the group consisting of : HP1, MRG15, MRG-1, cynCDY, Hrp3, dMi-2, CHD5, Swi6, and pdd3p.

97. The kit of claim 85, wherein the histone polypeptide is a polypeptide substrate for the histone-modification-specific binding domain.

98. The kit of claim 85, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHR (SEQ ID NO:1).

99. The kit of claim 85, wherein, wherein the histone polypeptide is an H3 polypeptide comprising the amino acid sequence set forth as ARTKQTARKSTGGKAPRKQLATKAARKSAP (SEQ ID NO:18).

100. The kit of claim 85, wherein the histone polypeptide is an H4 polypeptide comprising the amino acid sequence set forth as SGRGKGGKGLGKGGAKRHRKVLRDNIQGIT (SEQ ID NO:2).

101. The kit of claim 85, wherein the fusion protein reporter further comprises a targeting polypeptide, associated with the fusion protein.

102. The kit of claim 101, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand and a nuclear localization sequence (NLS), nuclear export signal (NES), plasma membrane targeting signal, a histone binding protein, and a nuclear protein.

103. A method for producing a fusion protein reporter comprising

providing an isolated nucleic acid molecule, wherein the isolated nucleic acid molecule is operably linked to a promoter encoding a fusion protein reporter comprising a core comprising a histone-modification-specific binding domain conjugated to a histone polypeptide, wherein the core is flanked by protein moieties, capable of being labeled with donor and acceptor fluorescent molecules, or a fragment thereof, and

expressing the nucleic acid molecule in an expression system.

104. The method of claim 103, further comprising:

isolating the fusion protein reporter or the fragment thereof from the expression system.

105. A fusion protein reporter, comprising a polypeptide encoded by a nucleic acid comprising a nucleotide sequence set forth as SEQ ID NO:4, wherein the fusion protein reporter is a yGcn5-based histone acetylation reporter.

106. The fusion protein reporter of claim 105, wherein the polypeptide comprises an amino acid sequence set forth as SEQ ID NO:5.

107. A fusion protein reporter, comprising a polypeptide encoded by a nucleic acid comprising a nucleotide sequence set forth as SEQ ID NO:6, wherein the fusion protein reporter is a TAFAB-based histone acetylation reporter.

108. The fusion protein reporter of claim 107, wherein the polypeptide comprises an amino acid sequence set forth as SEQ ID NO:7.

109. A fusion protein reporter comprising,

a core comprising an acetylation-modification-specific binding domain conjugated to a substrate polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties.

110. The fusion protein reporter of claim 109, wherein the acetylation-modification specific binding domain is conjugated to the polypeptide with a linker molecule.

111. The fusion protein reporter of claim 109, further comprising one or more additional acetylation-modification-specific binding domains.

112. The fusion protein reporter of claim 109, wherein the substrate polypeptide is tubulin or p53.

113. The fusion protein reporter of claim 109, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

114. The fusion protein reporter of claim 109, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

115. The fusion protein reporter of claim 109, wherein the acetylation-modification-specific binding domain is a bromodomain.

116. The fusion protein reporter of claim 115, wherein the bromodomain is selected from the group consisting of: Gcn5, $TAF_{II}250$, P/CAF, CBP, BRG1, Swi2, and Sth1.

117. The fusion protein reporter of claim 109, wherein the polypeptide is a polypeptide substrate for the acetylation-modification-specific binding domain.

118. The fusion protein reporter of claim 109, further comprising a targeting polypeptide, associated with the fusion protein.

119. The fusion protein reporter of claim 118, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand, a nuclear localization sequence (NLS), a nuclear export signal (NES), a plasma membrane targeting signal, p53, and tubulin.

120. An expression vector comprising an expression cassette encoding a fusion protein reporter of claim 109.

121. A fusion protein reporter comprising,

a core comprising a methylation-modification-specific binding domain conjugated to a substrate polypeptide, wherein the core is flanked by donor and acceptor fluorescent moieties.

122. The fusion protein reporter of claim 121, wherein the methylation-modification specific binding domain is conjugated to the polypeptide with a linker molecule.

123. The fusion protein reporter of claim 121, further comprising one or more additional methylation-modification-specific binding domains.

124. The fusion protein reporter of claim 121, wherein the donor fluorescent moiety is selected from the group consisting of cyan fluorescent protein (CFP), enhanced cyan fluorescent protein (ECFP), and A206K mutants thereof.

125. The fusion protein reporter of claim 121, wherein the acceptor fluorescent moiety is selected from the group consisting of yellow fluorescent protein (YFP), enhanced yellow fluorescence protein (EYFP), Citrine, Venus, and A206K mutants thereof.

126. The fusion protein reporter of claim 121, wherein the polypeptide is a polypeptide substrate for the methylation-modification-specific binding domain.

127. The fusion protein reporter of claim 121, further comprising a targeting polypeptide, associated with the fusion protein.

128. The fusion protein reporter of claim 127, wherein the targeting polypeptide is selected from the group consisting of a receptor ligand, a nuclear localization sequence (NLS), a nuclear export signal (NES), and a plasma membrane targeting signal.

129. An expression vector comprising an expression cassette encoding a fusion protein reporter of claim 121.